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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,739	07/28/2003	Gila Maor	26243	4122

7590 06/15/2007

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1651	

MAIL DATE	DELIVERY MODE
06/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,739	MAOR, GILA	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-107* is/are pending in the application.

4a) Of the above claim(s) *12,13,15,16 and 24-103* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11,14,17-23 and 104-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 and 11-107 are currently pending. The cancellation of claim 10 in the 3/15/07 paper is acknowledged.

Election/Restrictions

On 4/6/06, Examiner Lankford sent a requirement for restriction, to which applicants replied on 6/5/06. Upon reconsideration and in view of applicant's comments regarding the 4/6/06 requirement, Examiner Lankford sent a replacement requirement for restriction on 8/23/06. In response to this second requirement, applicants elected Group I, claims 1-23 and 104-107, and the species "IGF" in replies received 10/18/06 and 3/15/07, respectively. These elections were not explicitly indicated by applicant as being with or without traverse. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, however, the elections have been treated as elections without traverse (MPEP § 818.03(a)).

Claims 24-103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 12, 13, 15, and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the replies filed on 10/18/06 and 3/15/07.

Examination on the merits will commence at this time on claims 1-9, 11, 14, 17-23, and 104-107, to the extent they read on the elected species where applicable.

Information Disclosure Statement

The listing or recitation of references in the specification (as, for example, at pages 6, 34-37, 39, 40, 42, and 50-52 of the as-filed specification) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

The drawings are objected to because the photographs in Figures 1-3 and 6-9 are dark and unintelligible. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are

not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

It is noted that applicant has included color figures. Color photographs and color drawings are not accepted, however, unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Specification

The abstract of the disclosure is objected to because it is less than 50 words and contains numerous phrases that can be implied. Furthermore, the abstract does not sufficiently describe the invention. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper content, language, and format for an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and **should include that which is new in the art to which the invention pertains**. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for

making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of **50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. **The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.**

The language should be clear and concise and should not repeat information given in the title. **It should avoid using phrases which can be implied**, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co.*, Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See M.P.E.P. § 2163.02. In this case, the skilled artisan would not have reasonably concluded at the time of the invention that applicant was in possession of the entire invention as claimed.

In this case, claim 6 is drawn to a method of making cultured chondrocytes comprising culturing chondrocytes isolated from mandibular condyle "using culturing conditions devoid of a three dimensional support." The working example at page 44, lines 19-23, of the specification, however, clearly teaches that the chondrocytes are plated in "35mm six-well culture dishes." Culture dishes are three-dimensional (as, indeed, are all objects), and chondrocytes cannot grow without some solid support. Applicants have not shown possession of a method of making chondrocytes in which the culturing step is truly devoid of a three-dimensional support. Similarly, claim 8 requires in one embodiment that the method be conducted without "a polymer scaffold," a term that encompasses tissue culture polycarbonate plastic.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-9, 11, 14, 17-21, 23, and 104-107 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhalerao et al. (1995, *Tissue and Cell* 27: 369-382; reference U).

Bhalerao teaches incubating mouse mandibular condyles in DMEM/F-12 containing 0.1% collagenase, a protease, and agitating the tissue to liberate cells into the medium (page 370, column 2, under "Preparation of cell suspension"). Bhalerao teaches pooling the liberated cells (which include chondrocytes, osteocytes, and

numerous intermediate cell types; see page 370, column 2, under "Transfections"), pelleting them (*i.e.*, isolating them from the suspension medium) and culturing them in fresh medium for 3 passages over 9 days (*ibid.*). Bhalerao does not indicate that the cells are cultured in medium containing serum or any other added growth factors, including IGF-1 (claims 11, 14, and 17), and Bhalerao does not indicate that the culture flasks are coated with any biomolecule (*ibid.*), including polypeptides, ECM components, collagens, or fibronectin (claim 9). Bhalerao's culturing takes place in a culture flask, not on a bead matrix, gel, or semi-solid substance (claim 8). It is noted for the record that purification of the chondrocytes is not required by any of the cited claims.

Claims 1-5, 7-9, 14, 17-19, 23, and 104-107 are rejected under 35 U.S.C. 102(b) as being anticipated by Landesberg et al. (1995, *Calcified Tissue International* 56: 71-77; reference V).

Landesberg teaches incubating calf mandibular condyles first in F-12 medium containing 0.1% trypsin (a protease) and then in F-12 medium containing 0.2% collagenase (a protease), and agitating the tissue to liberate cells into the medium (page 71, column 1, under "Isolation of Mandibular Condylar Cells [MCCs]"). Landesberg teaches filtering the cells and collecting them by centrifugation (*i.e.*, isolating them from the protease medium) before culturing them (*ibid.*). Landesberg teaches that the MCCs isolated by their procedure comprise hypertrophic chondrocytes (Abstract; page 75, column 2, paragraph 3). Landesberg does not indicate that the cells are cultured in medium containing IGF-1 (claims 14, and 17), and Landesberg does not indicate that the culture flasks are coated with any biomolecule (*ibid.*), including

polypeptides, ECM components, collagens, or fibronectin (claim 9). Landesberg's culturing takes place in a culture dish, not on a bead matrix, gel, or semi-solid substance (claim 8). It is noted for the record that purification of the chondrocytes is not required by any of the cited claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7-9, 11, 14, 17-23, and 104-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhalerao et al. (reference U) taken in view of Palmer et al. (2002, *Arthritis Research* 4: 226-231; obtained online and including supplementary material, 8 pages total; reference W).

Bhalerao teaches incubating mouse mandibular condyles in DMEM/F-12 containing 0.1% collagenase, a protease, and agitating the tissue to liberate cells into the medium (page 370, column 2, under "Preparation of cell suspension"). Bhalerao teaches pooling the liberated cells (which include chondrocytes, osteocytes, and numerous intermediate cell types; see page 370, column 2, under "Transfections"), pelleting them (*i.e.*, isolating them from the suspension medium) and culturing them in fresh medium for 3 passages over 9 days (*ibid.*). Bhalerao does not indicate that the cells are cultured in medium containing serum or any other added growth factors, including IGF-1 (claims 11, 14, and 17), and Bhalerao does not indicate that the culture

flasks are coated with any biomolecule (*ibid.*), including polypeptides, ECM components, collagens, or fibronectin (claim 9). Bhalerao's culturing takes place in a culture flask, not on a bead matrix, gel, or semi-solid substance (claim 8). It is noted for the record that purification of the chondrocytes is not required by any of the cited claims.

Bhalerao does not teach passaging their cells 4 times, as required by claim 22.

Palmer teaches that chondrocytes may be subcultured several times (page 6, first paragraph under "Supplementary material") and that chondrocytes at passage 3 are equivalent in experiments to those at passage 5 (compare Figures 1 and 2).

A person of ordinary skill in the art would have had a reasonable expectation of success in passaging the cells of Bhalerao 4 times because Palmer teaches that chondrocytes may be passaged at least 5 times. The skilled artisan would have been motivated to passage the cells of Bhalerao 4 times for the expected benefit of increasing the number of cells generated from a single condyle.

The selection of passage number would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Palmer teaches that 3 passages and 4 passages are functionally equivalent in terms of chondrocyte culturing. A holding of obviousness over the cited claims is therefore clearly required. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart